



Clinical trial results:

A Single Arm, Multi-Center, International, Continuation Trial of Recombinant Humanized Antibody Herceptin® (Trastuzumab) in Patients with HER2-Overexpressing Tumors

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2007-000348-28 |
| Trial protocol | DE PT FR |
| Global end of trial date | 11 February 2015 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 01 November 2019 |
| First version publication date | 01 November 2019 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | BO15943 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02721641 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070 |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 11 February 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 11 February 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objectives of the study were to provide Herceptin IV to subjects with HER2-overexpressing disease following completion of any global Roche sponsored Herceptin study; to follow long-term outcomes in subjects who were being treated with Herceptin IV; and to follow long-term overall safety with Herceptin.

Protection of trial subjects:

All subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 15 June 1999 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 7 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Germany: 17 |
| Country: Number of subjects enrolled | Australia: 8 |
| Country: Number of subjects enrolled | New Zealand: 1 |
| Country: Number of subjects enrolled | Spain: 5 |
| Country: Number of subjects enrolled | Belgium: 1 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | Portugal: 2 |
| Country: Number of subjects enrolled | Hungary: 2 |
| Country: Number of subjects enrolled | Serbia: 6 |
| Country: Number of subjects enrolled | Russian Federation: 4 |
| Country: Number of subjects enrolled | Panama: 1 |
| Country: Number of subjects enrolled | Poland: 3 |
| Country: Number of subjects enrolled | Israel: 2 |
| Country: Number of subjects enrolled | China: 3 |
| Country: Number of subjects enrolled | Korea, Republic of: 10 |
| Country: Number of subjects enrolled | France: 1 |
| Country: Number of subjects enrolled | Guatemala: 1 |

| | |
|------------------------------------|----|
| Worldwide total number of subjects | 69 |
| EEA total number of subjects | 33 |

Notes:

| Subjects enrolled per age group | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 45 |
| From 65 to 84 years | 24 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects with any indication who had, at least, stable disease while receiving Herceptin intravenous (IV) at the end of the lead-in study were eligible for this study.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|-----------|
| Arm title | Herceptin |
|-----------|-----------|

Arm description:

Subjects received intravenous (IV) Herceptin until disease progression, unacceptable toxicity, death, or decision by the investigator or subject to discontinue treatment. Herceptin was administered at the discretion of the investigator as either 2 milligrams per kilogram (mg/kg) once weekly (first dose as a 4-mg/kg loading dose) or 6 mg/kg every 3 weeks (first dose as an 8-mg/kg loading dose) via IV infusion over 90 minutes.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Herceptin |
| Investigational medicinal product code | |
| Other name | Trastuzumab |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received IV Herceptin until disease progression, unacceptable toxicity, death, or decision by the investigator or subject to discontinue treatment. Herceptin was administered at the discretion of the investigator as either 2 mg/kg once weekly (first dose as a 4-mg/kg loading dose) or 6 mg/kg every 3 weeks (first dose as an 8-mg/kg loading dose) via IV infusion over 90 minutes.

| Number of subjects in period 1 | Herceptin |
|------------------------------------|-----------|
| Started | 69 |
| Completed | 0 |
| Not completed | 69 |
| Death | 1 |
| Refused Treatment | 3 |
| Drug Commercially Available | 12 |
| Not Specified | 15 |
| Adverse Event/Intercurrent Illness | 1 |
| Withdrawal by Subject | 1 |
| Lost to follow-up | 1 |
| Insufficient Therapeutic Response | 35 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Herceptin |
|-----------------------|-----------|

Reporting group description:

Subjects received intravenous (IV) Herceptin until disease progression, unacceptable toxicity, death, or decision by the investigator or subject to discontinue treatment. Herceptin was administered at the discretion of the investigator as either 2 milligrams per kilogram (mg/kg) once weekly (first dose as a 4-mg/kg loading dose) or 6 mg/kg every 3 weeks (first dose as an 8-mg/kg loading dose) via IV infusion over 90 minutes.

| Reporting group values | Herceptin | Total | |
|------------------------|-----------|-------|--|
| Number of subjects | 69 | 69 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--|---------|----|--|
| Age Continuous | | | |
| Age was the only demographic variable collected for the study and was only collected from 32 subjects. | | | |
| Units: years | | | |
| arithmetic mean | 58.0 | | |
| standard deviation | ± 11.00 | - | |
| Gender, Customized | | | |
| Gender data were not collected. To submit results, additional estimated data were entered. | | | |
| Units: Subjects | | | |
| Female | 69 | 69 | |
| Male | 0 | 0 | |

End points

End points reporting groups

| | |
|--|-----------|
| Reporting group title | Herceptin |
| Reporting group description: | |
| Subjects received intravenous (IV) Herceptin until disease progression, unacceptable toxicity, death, or decision by the investigator or subject to discontinue treatment. Herceptin was administered at the discretion of the investigator as either 2 milligrams per kilogram (mg/kg) once weekly (first dose as a 4-mg/kg loading dose) or 6 mg/kg every 3 weeks (first dose as an 8-mg/kg loading dose) via IV infusion over 90 minutes. | |

Primary: On-Study Duration on Trial Treatment

| | |
|--|---|
| End point title | On-Study Duration on Trial Treatment ^[1] |
| End point description: | |
| Analysis was performed on all enrolled subjects | |
| End point type | Primary |
| End point timeframe: | |
| From date of enrollment until death or premature withdrawal (maximum 7.4 years of follow-up) | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive analyses were performed for this end point.

| | | | | |
|-------------------------------|-------------------|--|--|--|
| End point values | Herceptin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 69 | | | |
| Units: days | | | | |
| median (full range (min-max)) | 386.0 (1 to 2697) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Drop in Left Ventricular Ejection Fraction (LVEF) Below 45 Percent (%)

| | |
|--|---|
| End point title | Number of Subjects with Drop in Left Ventricular Ejection Fraction (LVEF) Below 45 Percent (%) ^[2] |
| End point description: | |
| All enrolled subjects with available LVEF data were included in the analysis. | |
| End point type | Primary |
| End point timeframe: | |
| From date of enrollment until disease progression, death, or premature withdrawal; assessed per investigator discretion (maximum 7.4 years of follow-up) | |

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive analyses were performed for this end point.

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | Herceptin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 | | | |
| Units: Subjects | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Withdrawn from Study Because of LVEF Dysfunction

| | |
|-----------------|--|
| End point title | Number of Subjects Withdrawn from Study Because of LVEF Dysfunction ^[3] |
|-----------------|--|

End point description:

LVEF dysfunction was defined as low LVEF measured on two consecutive assessments, with the second assessment performed after 3 weeks of study medication being withheld. Low LVEF included values less than or equal to 39% or values between 40% and 45% (inclusive) with a decrease of 10 or more percentage points from Baseline. All enrolled subjects with available LVEF data were included in the analysis.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From date of enrollment until death or premature withdrawal (maximum 7.4 years of follow-up)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive analyses were performed for this end point.

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | Herceptin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 | | | |
| Units: Subjects | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

From date of enrollment until disease progression, unacceptable toxicity, death, or decision by the investigator or subject to discontinue treatment (up to approximately 7.4 years)

Adverse event reporting additional description:

Only serious adverse events were collected during the trial. Terms were reported verbatim as provided by the reporter and were not re-coded. Analysis was performed on all enrolled subjects.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|-----------------|
| Dictionary name | Global Database |
|-----------------|-----------------|

| | |
|--------------------|-----|
| Dictionary version | N/A |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Herceptin |
|-----------------------|-----------|

Reporting group description:

Subjects received IV Herceptin until disease progression, unacceptable toxicity, death, or decision by the investigator or subject to discontinue treatment. Herceptin was administered at the discretion of the investigator as either 2 mg/kg once weekly (first dose as a 4-mg/kg loading dose) or 6 mg/kg every 3 weeks (first dose as an 8-mg/kg loading dose) via IV infusion over 90 minutes.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: This study did not collect non-serious adverse event information.

| Serious adverse events | Herceptin | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 69 (15.94%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Fibula fracture | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower limb fracture | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Pain management | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| | | | |
|---|----------------|--|--|
| Non-serious adverse events | Herceptin | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 12 August 1998 | The protocol was updated to reflect a change from subjects with HER2-overexpressing breast cancer to subjects with HER2-overexpressing tumours as a result of the expansion of the development program for Herceptin; and no further chemotherapy was allowed to be taken concomitantly with Herceptin. |
| 18 October 2000 | The protocol was updated with all product-related information according to the Summary of Product Characteristics as a result of the approval of Herceptin in August 2000 by the European Agency for the Evaluation of Medicinal Products, including the possibility for subjects to receive paclitaxel in combination with Herceptin; participation in the study was limited to subjects with breast cancer; the dosing regimen was updated to include details for subjects who were receiving Herceptin IV in the lead-in protocol and subjects who were not previously treated with Herceptin IV. |
| 12 February 2007 | The protocol was updated as follows: subjects from all global Roche-sponsored Herceptin trial (all indications) were able to enroll into the study and would be provided with Herceptin even if it was commercially available in their country; subjects could continue treatment with the same anticancer drugs, at the same dose and schedule, they received in the lead-in protocol, as long as the treatment was still ongoing at the completion of the lead-in protocol and was still considered beneficial for the subject; the informed consent form was amended to include safety information relating to possible effects on reproduction or fetal development, risks and side effects, and the addition of regular heart function monitoring; the case report form (CRF) was changed to include date of visit, date of birth, and concomitant cancer treatments; left ventricular ejection fraction (LVEF) values were to be collected; the study completion page of the CRF was changed; the study completion date was replaced by date of last dose, date of progression, and date of death; the units of initial dose was changed from mg/kg to mg. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Age data were only collected for 22 subjects aged 18–64 yrs. and 10 subjects aged 65–84 yrs. Gender data were not collected. To submit results, additional estimated data were entered in the "Trial Information" and "Gender" sections.

Notes: